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HIP

The prevalence and treatment of osteoporosis in patients undergoing total hip arthroplasty and the levels of biochemical markers of bone turnover

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Aims

Osteoporosis is common in total hip arthroplasty (THA) patients. It plays a substantial factor in the surgery's outcome, and previous studies have revealed that pharmacological treatment for osteoporosis influences implant survival rate. The purpose of this study was to examine the prevalence of and treatment rates for osteoporosis prior to THA, and to explore differences in osteoporosis-related biomarkers between patients treated and untreated for osteoporosis.

Methods

This single-centre retrospective study included 398 hip joints of patients who underwent THA. Using medical records, we examined preoperative bone mineral density measures of the hip and lumbar spine using dual energy X-ray absorptiometry (DXA) scans and the medications used to treat osteoporosis at the time of admission. We also assessed the following osteoporosis-related biomarkers: tartrate-resistant acid phosphatase 5b (TRACP-5b); total procollagen type 1 amino-terminal propeptide (total P1NP); intact parathyroid hormone; and homocysteine.

Results

The prevalence of DXA-proven hip osteoporosis (T-score ≤ -2.5) among THA patients was 8.8% (35 of 398). The spinal osteoporosis prevalence rate was 4.5% (18 of 398), and 244 patients (61.3%; 244 of 398) had osteopenia (-2.5 < T-score ≤ -1) or osteoporosis of either the hip or spine. The rate of pharmacological osteoporosis treatment was 22.1% (88 of 398). TRACP-5b was significantly lower in the osteoporosis-treated group than in the untreated group ($p < 0.001$).

Conclusion

Osteoporosis is common in patients undergoing THA, but the diagnosis and treatment for osteoporosis were insufficient. The lower TRACP-5b levels in the osteoporosis-treated group — that is, osteoclast suppression — may contribute to the reduction of the postoperative revision rate after THA.

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Keywords: Bone mineral density, TRACP-5b, Total P1NP

Article focus

- The prevalence of osteoporosis and osteopenia in prospective total hip arthroplasty (THA) patients.
- The low rate of pharmacological treatment for osteoporosis in THA patients.
- The difference in osteoporosis-related biomarkers between treated and untreated groups.

Key messages

- Osteoporosis is common in THA patients.

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- Pharmacological treatment for THA patients is insufficient.
- Osteoporosis-related biomarkers are significantly lower in THA patients than in untreated groups ($p < 0.001$).

Strengths and limitations

- This is a unique study in the medical literature.
- Few studies have investigated osteoporosis-related biomarkers.
- The clinical significance of the results requires further investigation.
- Treatment of osteoporosis does not always follow standard operating procedure for consensus of treating osteoporosis based on Fracture Risk Assessment Tool/dual energy X-ray absorptiometry score.

Introduction

Total hip arthroplasty (THA) provides excellent functional recovery for patients with hip disorders, such as hip osteoarthritis (OA) and femoral head necrosis. The number of THAs performed is increasing globally,[1,2] and this trend likely contributes to the increasing incidence of periprosthetic fracture,[3-5] aseptic loosening, and periprosthetic joint infection,[6] an uncommon but potentially disabling side-effect.

Osteoporosis is common before THA, especially in elderly patients,[7,8] and the condition is undertreated and undervalued preoperatively.[9] Previous studies suggest that osteoporosis is a risk factor for aseptic loosening and periprosthetic fractures, which are common causes of revision after THA.[10] Randomized controlled trials (RCTs) indicate that osteoporosis medication prevents periprosthetic bone loss after THA.[11] Despite this awareness, bone mineral density (BMD) and bone quality are not routinely investigated, and preoperative osteoporosis is not treated preoperatively.[12] Given that the preoperative optimization of BMD and bone quality may help to mitigate these complications, they are important perioperative considerations; however, they have been underemphasized to date.[9]

Various osteoporosis-related biomarkers have been identified and measured to help assess bone quality.[13,14] The relationship between these biochemical markers and osteoporotic fractures has been previously reported in osteoporosis patients.[15-17] However, few reports exist on the relationships between such biomarkers in preoperative THA patients.[18,19] The purpose of this study was to investigate the prevalence and treatment rates of osteoporosis and compare osteoporosis-related biomarkers in patients treated and untreated for osteoporosis preoperatively.

Methods

Study design. This single-centre retrospective study was performed according to the principles of the Declaration of Helsinki.[20] This study is still ongoing, and all patients whose data were included in this manuscript provided written informed consent through a preoperative informed consent process to publish the case details.

Study population. This study included 487 patients who underwent primary THA between July 2017 and December 2020. The mean age was 65.5 years (standard deviation (SD) 11.8). A total of 24 hip joints with femoral neck fractures were excluded from the analysis because the BMD measurement of the displaced femoral neck was not appropriate for accurately measuring BMD. In total, 65 hip joints without both BMD and osteoporosis-related biomarkers were also excluded from the analysis. Overall, 398 patients with a mean age of 65.1 years (SD 11.6) who underwent THA between July 2017 and December 2020 were included (Figure 1). Table I presents the demographic details of the study group.

We reviewed electronic medical records retrospectively to obtain preoperative pharmacological osteoporosis treatment data.

Preoperative measurement. We focused on preoperative BMD and osteoporosis-related biomarkers, as these data have been collected routinely since July 2017 to assess preoperative osteoporosis and bone quality in all patients undergoing primary THA. Among the 487 hip joints, 398 (82%) included data for both preoperative BMD and the following osteoporosis-related biomarkers: serum tartrate-resistant acid phosphatase 5b (TRACP-5b); total procollagen type 1 amino-terminal propeptide (total P1NP); intact parathyroid hormone (intact PTH); and homocysteine. The preoperative BMDs of the operation side

Table I. Baseline clinical and demographic characteristics.

Characteristic	Data
Patients, n	398
Mean age, yrs (SD)	65.1 (11.6)
Sex, n	
Male	68
Female	330
Preoperative diagnosis, n	
DDH-OA	308
Osteonecrosis of the femoral head	48
Primary OA	17
Rapidly destructive coxarthrosis, a rare syndrome that typically involves the rapid and aggressive destruction of the unilateral hip joint	15
Rheumatoid arthritis	7
Others	3

DDH, developmental dysplasia of the hip; OA, osteoarthritis; SD, standard deviation.

Table II. Prevalence of osteopenia and osteoporosis.

Location	Osteoporosis, n (%)	Osteopenia, n (%)	Osteopenia or osteoporosis, n (%)
Hip (n = 398)	35 (8.7)	184 (46.2)	219 (55.0)
Spine (n = 398)	18 (4.5)	115 (28.9)	133 (33.4)
Hip or spine (n = 398)	46 (11.6)	198 (49.7)	244 (61.3)

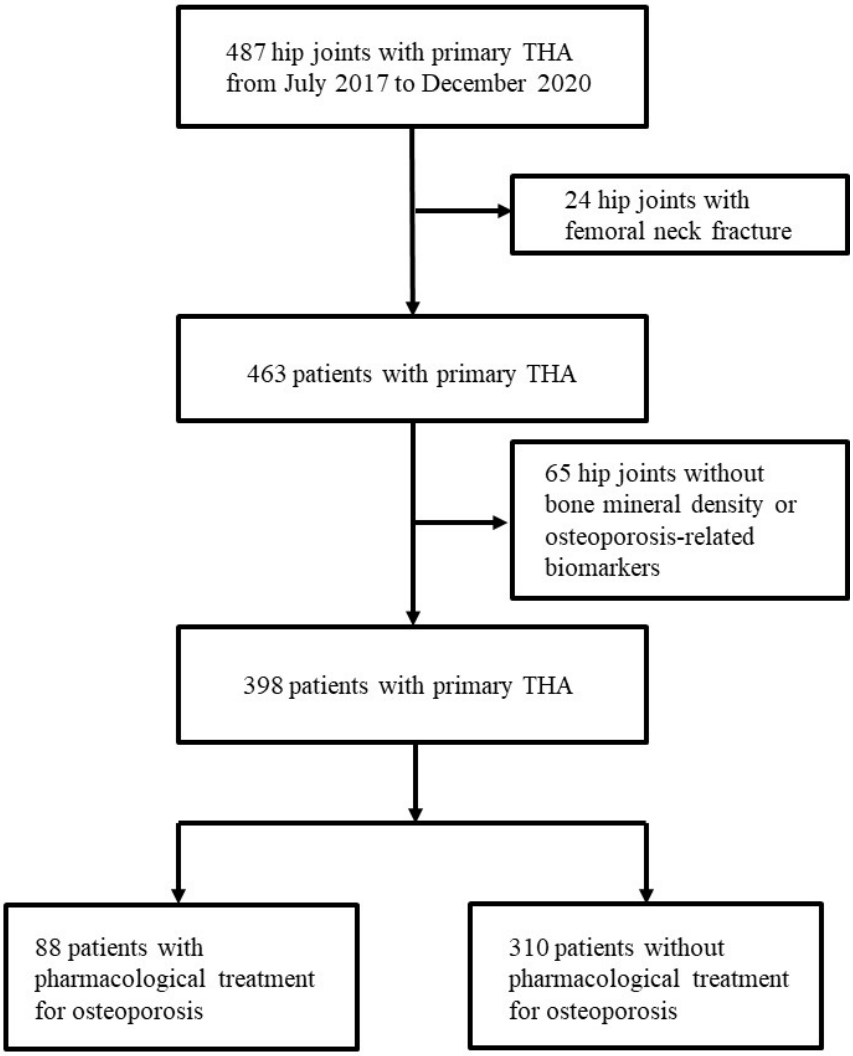

Fig. 1

Flowchart of patient selection. THA, total hip arthroplasty.

of the hip and spine were measured using dual-energy X-ray absorptiometry (DXA), with the results expressed as total hip and spine BMD. The T-score represents the number of SDs from the mean BMD of a young adult, with osteoporosis defined as a BMD T-score ≤ -2.5 and osteopenia as a T-score between -1 and -2.5, according to the criteria of the World Health Organization (WHO).[21]

Covariates. Patient background data (age, sex, height, weight, BMI, and preoperative diagnosis) were recorded.

Statistical analysis. Statistical analyses were performed using SPSS v27 (IBM, USA). Chi-squared tests were used to compare categorical values, and continuous variables were evaluated with independent-samples *t*-tests assuming unequal variance. A Pearson's rank correlation test was used to assess the linear correlation between osteoporosis-related biomarkers (TRACP-5b, total P1NP, intact PTH, and homocysteine) and hip T-scores. A p-value less than 0.05 were considered statistically significant.

Results

Prevalence and treatment rate of osteoporosis before THA. The mean T-score was -1.1 (SD 1.2) for the hip (Figure 2) and -0.19 (SD 1.6) for the lumbar spine (Figure 3). The cohort's mean hip Z-score and mean spine Z-score were positive, at 0.26 (SD 1.2) and 1.2 (SD 1.7), respectively. The prevalence of DXA-proven hip osteoporosis (T-score ≤ -2.5) and spinal osteoporosis was 8.7% (35 of 398) and 4.5% (18 of 398), respectively, and 244 patients (61.3%; 244 of 398) had osteopenia or osteoporosis of either the hip or spine (Figure 4, Table II).

The osteoporosis treatment rate was 22.1% (88 of 398; Table III). The treatment rate of osteoporosis in normal, osteopenia, and osteoporosis patients was 20.8% (48 of 231), 24.5% (26 of 106), and 26.2% (16 of 61), respectively (Figure 5). The breakdown of the therapeutic agents used for osteoporosis included 40 patients on vitamin D analogues (ten for alfacalcidol and 30 for

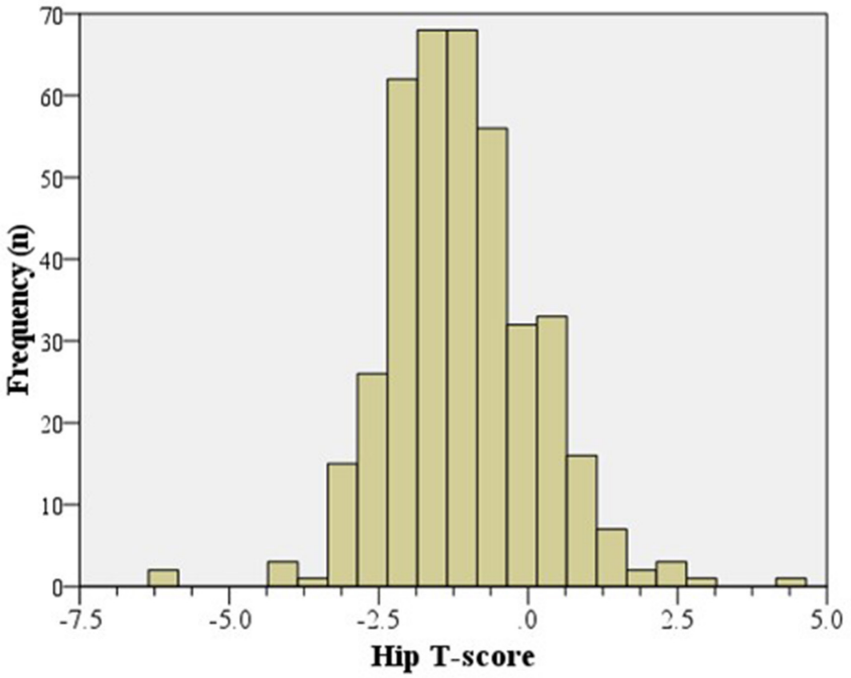

Fig. 2

Histogram showing the distribution of hip T-scores (n = 398).

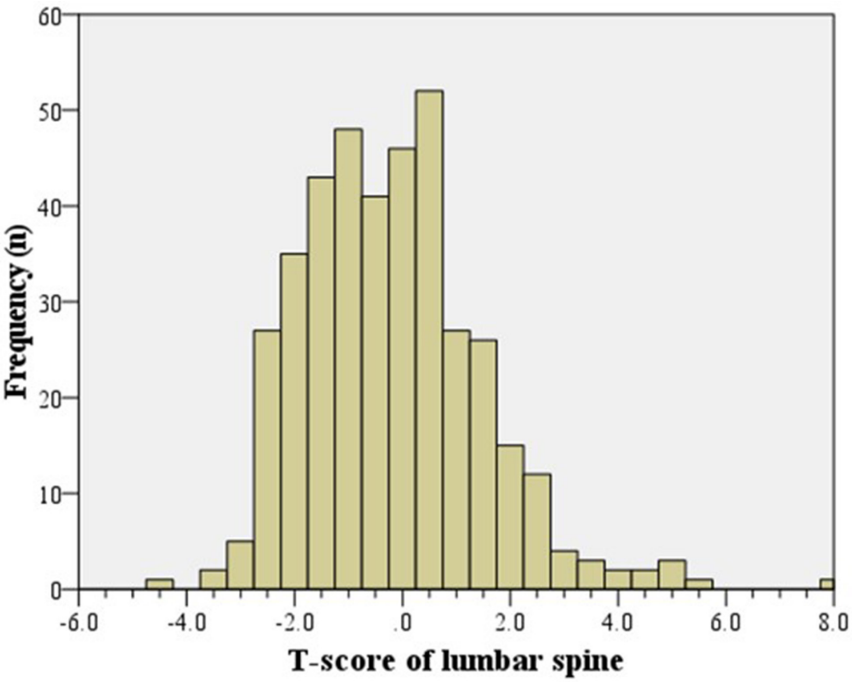

Fig. 3

Histogram showing the distribution of lumbar spine T-scores (n = 398).

eldecalcitol), 24 on bisphosphonates, eight on a combination of bisphosphonates and vitamin D analogues, six on selective oestrogen receptor modulators, seven on teriparatides, and three on denosumab.

Correlations between the continuous variables, hip T-score, and the osteoporosis-related biomarkers of serum TRACP-5b, total P1NP, intact PTH, and homocysteine were assessed using Pearson's rank correlation.

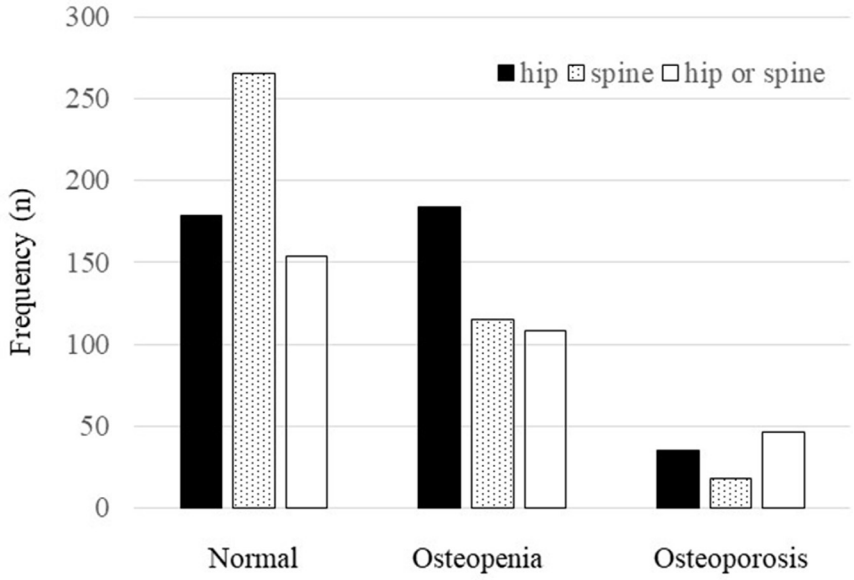

Fig. 4

Prevalence of osteoporosis and osteopenia.

A Pearson's test revealed a weak negative correlation between hip T-score and TRACP-5b ($r = -0.197$, $p < 0.001$) and total P1NP ($r = -0.121$, $p = 0.016$). The negative correlation was more pronounced when observed in the untreated group. No significant correlation was shown between hip T-score and the other biomarkers (Figure 6, Table IV).

Difference in osteoporosis-related biomarkers with and without treatment for osteoporosis. Of 398 patients, 88 were pharmacologically treated for osteoporosis and 310 were untreated. TRACP-5b was significantly lower in the osteoporosis-treated group than in the untreated group, despite no significant difference in hip T-scores between the two groups. The levels of other osteoporosis-related biomarkers were not significantly different between the groups (Table V).

Table III. Breakdown of preoperative osteoporosis drugs used for patients.

Medication	n
Vitamin D	
Alfacalcidol	10
Eldecalcitol	30
BP	24
BP + vitamin D	
BP + alfacalcidol	4
BP + eldecalcitol	4
SERM	6
Teriparatide	7
Denosumab	3
Total	88

BP, bisphosphonate; SERM, selective oestrogen receptor modulator.

Discussion

In our study, 244 patients (61.3%; 244 of 398) had osteopenia or osteoporosis of either the hip or spine according to WHO criteria. However, the treatment rate for osteoporosis was only 22.1% (88 of 398). Hip T-score had a weak negative correlation with TRACP-5b and total P1NP. TRACP-5b was significantly lower in the osteoporosis-treated group than in the untreated group, although no significant difference in hip T-score existed between the two groups.

We found low bone mass, defined as osteopenia or osteoporosis according to WHO criteria, in a large number (61.3%) of the patients before THA in our study. Lingard et al[8] found that 33% of patients in the UK awaiting arthroplasty for the lumbar spine and 37% for the proximal femur had low bone mass. Our results indicated a much higher prevalence of preoperative osteoporosis before THA than previously reported;[8] however, research has suggested that Japanese patients have an even higher prevalence of osteoporosis than other populations,[22] and our results are consistent with these previous reports.[7,8]

In our study group, pharmacological osteoporosis treatment was applied to only around one in five patients preoperatively, regardless of their BMD. Previous studies have also found osteoporosis to be common, underdiagnosed, and undertreated prior to joint arthroplasty.[9,23] Considering the treatment rates for hypertension (70% to 80%) in Japan,[24] the treatment rate for osteoporosis in our country is still low,[25] which suggests that physicians and orthopaedic surgeons may have been paying less attention to osteoporosis than to other chronic diseases. Preoperative information about bone status is particularly important in arthroplasty to avoid intraoperative fractures and other postoperative complications, including stem subsidence,[26] implant loosening,[27] and late periprosthetic fractures.[28]

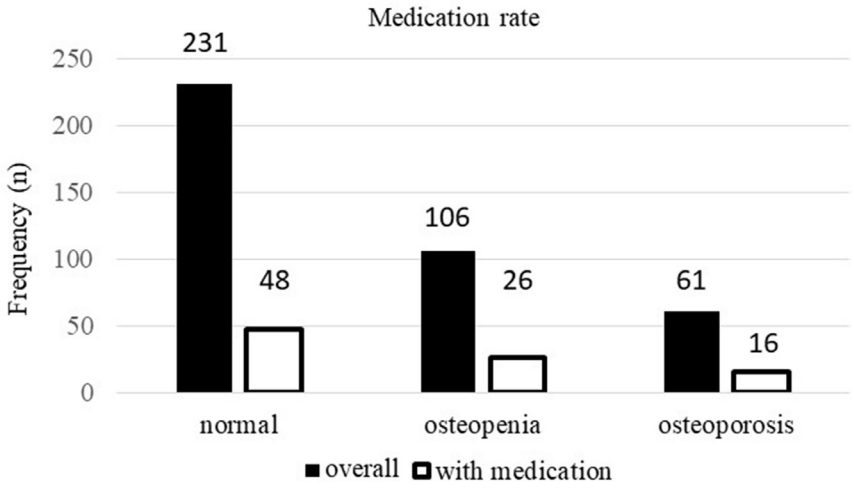

Fig. 5

The rate of pharmacological osteoporosis treatment in patients from the normal, osteopenia, and osteoporosis groups.

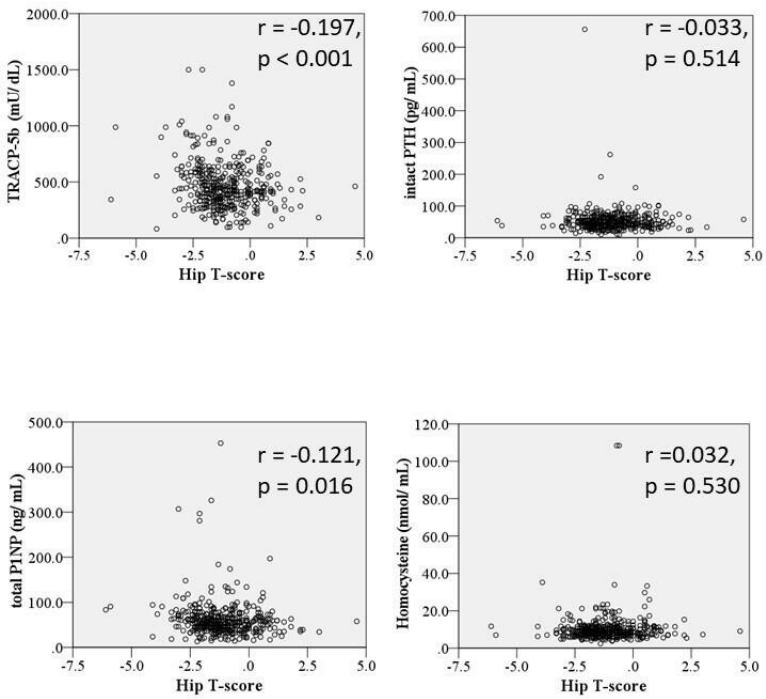

Fig. 6

Scatter diagrams showing the relationships between hip T-scores and osteoporosis-related biomarkers (tartrate-resistant acid phosphatase 5b (TRACP-5b), total procollagen type 1 amino-terminal propeptide (total P1NP), intact parathyroid hormone (PTH), and homocysteine). The total number of patients was 398. All p-values were calculated using Pearson's rank correlation. r = correlation coefficient.

The relationships between BMD and osteoporosis-related biomarkers have been studied previously,[29–32] and these factors have recently been related to gut microbiome.[33–35] However, patients undergoing THA have not been adequately studied regarding the relationships between BMD and osteoporosis-related biomarkers. Our results of correlations between hip T-score and osteoporosis-related biomarkers are consistent with previous reports.[29–32] Osteoporosis treatment cancels the correlation between osteoporosis-related biomarkers and BMD, and the same effect is thought to be caused in vivo. Previous reports include large-scale clinical studies showing that the use of bisphosphonates resulted in a statistically significant reduction in the postoperative revision rate after artificial joint arthroplasty,[36] and RCTs in which postoperative osteoporosis treatment suppressed

Table IV. Correlation coefficients between osteoporosis pharmacological treatment and osteoporosis-related biomarkers (r = correlation coefficient, n = 398).

	Medication					
	Yes (n = 88)		No (n = 310)		Overall (n = 398)	
Biomarker	r	p-value	r	p-value	r	p-value
TRACP-5b	-0.029	0.789	-0.261	< 0.001	-0.197	< 0.001
Total P1NP	-0.033	0.763	-0.189	< 0.001	-0.121	0.016
Intact PTH	0.047	0.662	-0.061	0.284	0.284	0.514
Homocysteine	0.205	0.056	0.017	0.761	0.032	0.530

Medication: whether patients are using osteoporosis medication.
P1NP, procollagen type 1 amino-terminal propeptide; PTH, parathyroid hormone; TRACP-5b, tartrate-resistant acid phosphatase 5b.

Table V. Changes in bone mineral density and osteoporosis-related biomarkers with and without pharmacological treatment for osteoporosis.

	Medication		
Variable	Yes (n = 88)	No (n = 310)	p-value*
Mean T-score of femoral neck (SD)	-1.3 (1.2)	-1.0 (1.2)	0.079
Mean T-score of lumbar spine (SD)	-0.5 (1.6)	-0.1 (1.7)	0.029
Mean TRACP-5b, mU/dl (SD)	393.6 (207.3)	490.0 (207.2)	< 0.001
Mean total P1NP, ng/ml (SD)	58.7 (64.3)	62.8 (30.8)	0.402
Mean homocysteine, nmol/ml (SD)	10.8 (5.3)	10.1 (8.9)	0.471
Mean intact PTH, pg/ml (SD)	50.9 (35.5)	53.1 (39.2)	0.625

Medication: whether patients are using osteoporosis medication.
*Independent-samples *t*-test.
P1NP, procollagen type 1 amino-terminal propeptide; PTH, parathyroid hormone; SD, standard deviation; TRACP-5b, tartrate-resistant acid phosphatase 5b.

the reduction in peri-implant BMD.[11] These results may be associated with low TRACP-5b levels — that is, osteoclast suppression — and further studies are warranted.

Our study has three limitations. First, the information about pharmacological osteoporosis treatment before THA was obtained retrospectively from electronic medical records. We did not prospectively investigate the treatment period, so the effect of medication on osteoporosis-related biomarkers could differ according to the treatment period. Regarding bisphosphonates, a previous report indicated that starting bisphosphonates six months before surgery and continuing three years after surgery is desirable.[37] Second, in most of our cases, pharmacological osteoporosis treatment was started by general practitioners or doctors in other departments, and the reasons for starting osteoporosis drugs are not clear. Third, changes in biomarker values may be different depending on the drug in the treatment group. However, we believe that our results regarding the severe osteoarthritic population provide valuable information. As the number of subjects increases, investigation into changes in biomarker values with each drug will be possible, and future research in this area is needed.

In conclusion, osteoporosis is common in patients undergoing THA, but the diagnosis and treatment for osteoporosis were insufficient. The lower TRACP-5b levels in the osteoporosis-treated group — that is, osteoclast suppression — may contribute to the reduction of the postoperative revision rate after THA.

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